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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/731,726	12/09/2003	Sergei Zolotukhin	4300.007897	5277

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EXAMINER	
SALVOZA, M FRANCO G	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 08/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/731,726	ZOLOTUKHIN ET AL.	
	Examiner	Art Unit	
	M. Franco Salvoza	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) *1-23, 25-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24, 31-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12/09/03* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/09/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-23, 25-30 were canceled. New claims 31-46 were added.

Claims 24, 31-46 are pending and under consideration.

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 24, 31-46 are rejected under 35 U.S.C. 102(b) as being anticipated by Tamayose et al. (1996) or, in the alternative, under 35 U.S.C. 103(a) as obvious over Tamayose et al. (1996).

Claim 24 recites a recombinant adeno-associated virus, prepared by applying a sample containing recombinant adeno-associated virus to an iodixanol gradient, and collecting said recombinant adeno-associated virus from said gradient.

Claim 31 recites a purified recombinant adeno-associated virus, prepared by applying a crude sample containing recombinant adeno-associated virus to at least a first matrix comprising:

heparin under conditions effective to permit binding of the virus to said first matrix; eluting the virus from the matrix, contacting the eluted virus with at least a first iodixanol gradient and collecting the virus.

Claim 32 recites a purified recombinant adeno-associated virus (rAAV) prepared by applying a crude sample containing rAAV to an iodixanol gradient and collecting the rAAV from said gradient.

Claim 33 recites a purified, high titer recombinant adeno-associated virus (rAAV) stock obtained by the steps of: i.) contacting a crude sample containing a population of rAAV particles with a heparin matrix under conditions effective to permit binding of the rAAv particles to the heparin; ii) removing non-bound particles from the first matrix by a selective first elution; iii) eluting the population of rAAV from the heparin matrix by a second elution; iv) subjecting the population of rAAv from step iii) to an iodixanol gradient; and v) collecting the rAAV from selected gradient fractions.

Claims 34-40 recite the rAAV stock of claim 33 wherein the first matrix is heparin agarose type 1; wherein the first matrix is heparin agarose type II-S; wherein the rAAV collected from selected gradient fractions is contacted with a hydrophobic matrix that interacts with hydrophobic species and collecting non-interacting virus eluted from the hydrophobic matrix; wherein the hydrophobic matrix comprises agarose; wherein the hydrophobic matrix comprises phenyl- agarose; wherein the stock is obtained by the steps of I-V further comprising contacting the collected virus from the first iodixanol gradient with a second iodixanol gradient and collecting the virus from said second iodixanol gradient; wherein the stock is obtained by the

steps of I-v further comprising applying the virus collected from the first iodixanol gradient to a first cesium chloride gradient, and collecting the virus from the first cesium chloride gradient.

Claims 41-46 further recite the rAAV stock of claim 36 wherein collecting the stock further comprises applying the virus from the hydrophobic matrix to a second iodixanol gradient and collecting the virus from the second iodixanol gradient; further comprising the step of applying the virus collected from the first cesium chloride gradient to a second cesium chloride equilibrium density gradient and collecting the virus from at least a first fraction of the second cesium chloride equilibrium density gradient; wherein the heparin matrix is comprised within an HPLC column; wherein the first iodixanol gradient comprises an about 15% iodixanol step, and about 25% iodixanol step, and about 40% iodixanol step, or an about 60% iodixanol step; wherein at least the first iodixanol gradient further comprises NaCl; wherein the virus is eluted from the first matrix with a composition comprising at least about IM NaCl.

Claims 24, 31-46 are all product-by-process claims reciting a recombinant adeno-associated virus, which are interpreted as product claims reciting a recombinant adeno-associated virus. The determination of patentability is based on the product itself, not its method of production. See MPEP § 2113.

Tamayose et al. (1996) teaches recombinant adeno-associated virus vectors for human gene therapy, prepared on a large scale (p. 507).

Where applicant claims a composition in terms of a characteristic not explicitly disclosed by the reference, a 35 U.S.C. 102/103 rejection is proper (See MPEP § 2112).

Claims 24, 31-46 are rejected under 35 U.S.C. 102(a) as being anticipated by Maxwell et al. (1997) or, in the alternative, under 35 U.S.C. 103(a) as obvious over Maxwell et al. (1997).

See the recitation to claims 24, 31-46 above. See also MPEP 2113.

Maxwell et al. teaches recombinant adeno associated vectors produced by transfecting NB324K cells through electroporation (p. 129).

Where applicant claims a composition in terms of a characteristic not explicitly disclosed by the reference, a 35 U.S.C. 102/103 rejection is proper (See MPEP § 2112).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 24, 31-46 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent 5,962,313.

Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 24, 31-46 recite a genus of recombinant adeno-associated virus that is anticipated by the species of claims 1-6 of U.S. Patent 5,962,313 reciting recombinant adeno-associated virions comprising a gene encoding a lysosomal enzyme operably linked to transcriptional and translational control elements.

Claims 24, 31-46 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 19-50, 51-57 of copending Application No. 10/651,828, claims 28, 29 of copending Application No. 11/043658, claims 38, 41, 44, 49-57, 62 of copending Application No. 10/267,117, claims 1, 8, 9, 16, 27-36, 38 of copending Application No. 10/519,812, claims 1-16 of copending Application No. 11/055,497, claims 23, 24 of copending Application No. 11/303,896, claims 1-33, 35-39, 43-46, 50, 58-61, 63, 64, 66, 67, 76, 103 of copending Application No. 10/513,059, claims 1-4, 6-40, 45-48, 54, 62-68 of copending Application No. 10/513,348.

Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 24, 31-46 recite a genus of recombinant adeno-associated virus that is anticipated by the species of the cited claims of the copending applications reciting recombinant adeno-associated virions comprising specific elements.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to M. Franco Salvoza whose telephone number is (571) 272-8410. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

M. Franco Salvoza
Patent Examiner
August 10, 2006

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